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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,251	12/12/2000	Guy Reed	21509-020 Div.	7325

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	18

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/735,251	REED ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,18,19 and 22-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9 and 10* is/are allowed.

6)☒ Claim(s) *18,19 and 22-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 12/02/02 (Paper No. 17), is acknowledged.

2. Claims 9, 10, 18, 19, and 22-33 are pending and under consideration.

3. In view of the amendment filed on 12/02/02 (Paper No. 17), only the following rejections remained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 18-19 and 22-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO:4 encoded by the DNA of SEQ ID NO:3 for generating antibodies diagnostic for activated platelets and for thrombus; does not reasonably provide enablement for any polypeptide "comprising" any antigenic fragment of SEQ ID NO: 4, wherein said fragment is at least 10 residues in length and wherein said fragment lacks a transmembrane domain in claim 18, any substantially pure polypeptide "comprising" any fragment of SEQ ID NO:4, wherein said polypeptide binds to MAb 3B2 (ATCC Designation No. CRL-11986) in claim 19, wherein the fragment is at least 20, 50, 60, 100, 200 or 300 residues in length in claims 22-33. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/20/02.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses only a single amino acid sequence (SEQ ID NO:4) encoded by a single nucleic acid sequence (SEQ ID NO:1) with a disclosed utility in generating antibodies diagnostic for activated platelets and for thrombus (e.g., page 7 at lines 25-27). The instant claims encompass in their breadth any polypeptide comprising a sequence at least 10, 20, 50, 60, 100, 200 or 300 residues in length of SEQ ID NO:4; *any* polypeptide comprising any "antigenic fragment" at least 10 residues in length, including those lacks a transmembrane domain or binds to MAb 3B2 antibody.

The term "comprising" in claims 18 and 19 is open-ended, it expand the amino acid fragments of SEQ ID NO: 4 to include additional non disclosed amino acids either or both N- and C termini of SEQ ID NO: 2 outside of the "at least 10, 20, 50, 60, 100, 200 or 300 residues in length". The instant claim language appears to encompass fragments. For example, claim 18 recites an antigenic fragment of SEQ ID NO: 4, wherein said fragment is at least 10 residues in length and lacks a transmembrane domain. Such a recitation does not require that the full length amino acid sequence set forth in SEQ ID NO:4; but rather encompasses any amino acid sequence

comprising either the full length of SEQ ID NO:4 or *any fragment*. However, the specification does not appear to have provided sufficient guidance as to which fragments of SEQ ID NO:4 associate with the platelet membrane and expressed by activated platelets. Neither does the specification appear to have provided any working examples of any functional fragments. Thus it would require undue experimentation of the skilled artisan to determine which fragments of SEQ ID NO:4 would have the function of the full length molecule.

Applicant's arguments, filed 12/02/02 (Paper No. 17), have been fully considered, but have not been found convincing.

Applicant contends that it is will within the skill of an average molecular biologist to make polypeptides which are shorter in length than the full-length protein and have the structural requirements defined by the amended claim. Applicant further submits that the specification discloses that such polypeptide can be generated by methods known to those skilled in the art (page 6, lines 29-31).

However, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various amino acids recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for the polypeptide activity. Without detailed direction as to which amino acid sequences are essential to the function of the polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of amino acid sequences encompassed by the instant claims would be expressed by activated platelets, other than the amino acid of SEQ ID NO:4.

Further, it is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. The specification does not teach which changes in the amino acid of SEQ ID NO:4 would not alter all the activities of the peptide. Therefore, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 4 is essential for maintain its biological activity and which changes can be made in the structure of SEQ ID NO: 4 and still maintained the same function.

Applicant asserts that claim 19 require a polypeptide that binds to Mab 3B2 and contains fragment of the sequence defined by SEQ ID NO:4. Applicant argues in conjunction with case law that a requirement of some experimentation by a skilled person does not preclude enablement; all that is required is that the amount of experimentation not be unduly extensive. Applicant argues that determining whether a polypeptide fragment of SEQ ID NO:4 binds to a

specific antibody is a simple test that is routinely carried out by those skilled in the art of the invention.

However, one skilled in the art at the time of the invention would not be able to predict which fragments will bind to the specific antibody. Consequently the skilled artisan would not know how to use the instant invention as broadly claimed. While experimental testing techniques using antibodies are available, it is not routine in the art to use such methods when the expectation of success is unpredictable based on the instant disclosure. Thus, it would require an undue amount of experimentation of one skilled in the art to practice the invention as broadly claimed. Further, the antibody binding is not seen as sufficiently limiting since an antibody epitope may be as small as 6-15 shared amino acid residues and places no limitations on the function of the protein containing the polypeptide sequence recognized.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

6. Claims 18-19 and 22-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/20/02.

Applicant is in possession of polypeptide of SEQ ID NO: 4 encoded by nucleic acid of SEQ ID NO:3.

Applicant is not in possession of any polypeptide "comprising" any antigenic fragment of SEQ ID NO: 4, wherein said fragment is at least 10 residues in length and wherein said fragment lacks a transmembrane domain in claim 18, any substantially pure polypeptide "comprising" any fragment of SEQ ID NO:4, wherein said polypeptide binds to MAb 3B2 (ATCC Designation No. CRL-11986) in claim 19, wherein the fragment is at least 20, 50, 60, 100, 200 or 300 residues in length in claims 22-33.

Applicant's arguments, filed 12/02/02 (Paper No. 17), have been fully considered, but have not been found convincing.

Applicant argues that the specification describes the structural and functional properties of a representative number of examples so as to show that Applicants were in possession of the claimed genus. Applicant provides an example wherein the polypeptides of APP-2 bind to Mab

3B2 are located in the extracellular portion of the protein of the activated platelets. Applicant further asserts that the specification describes at least three examples of fragments that bind to MAb 3B2: fragments that lack a transmembrane domain of SEQ ID NO:4, fragments that lack an intracellular domain of APP-2, and APP-2 fragment that lack both transmembrane and intracellular domains (page 7, lines 1-16).

Applicant has disclosed only amino acid of SEQ ID NO: 4 and the deleted transmembrane domain and/or intracellular domain of SEQ ID NO: 4; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993).

Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of fragments, wherein the fragment has at least 10, 20, 50, 60 100, 200 or 300 residues in length which retain functional features essential to the instant invention.

7. Claims 9-10 are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9307.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
August 25, 2003

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